Lactic Acid Derivatives. 4,4,6-Trimethyl-2-(1-hydroxyethyl)-5,6-dihydro-1,3,4H-oxazine[1]

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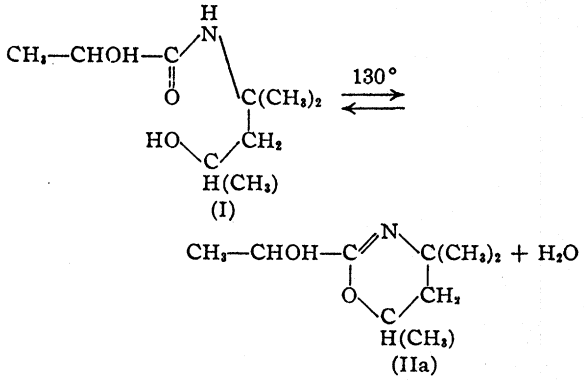
Although hydroxy alkyl amides of lactic acid are generally prepared from methyl lactate without difficulty[2] the attempted preparation of N-(1,1-dimethyl-3-hydroxybutyl)-lactamide (I), from 4-methyl-4-amino-2-pentanol and methyl lactate has led instead to the formation (at 130°) of an anhydro compound of empirical formula $C_9H_{17}O_2N$ (II), which we believe to be 4,4,6-trimethyl-2-(1-hydroxyethyl)-5,6-dihydro-1,3,4H-oxazine (IIa).



The lactamide (I) was obtained in 12% yield by crystallization from the aminolysis mixture and also by reversal of the above reaction. The evidence on which we assign the structure (IIa) is (1) empirical formula, (2) neutralization equivalent, (3) hydroxyl analysis, (4) conversion of (II) to (I) by an equivalent of water, (5) analysis of the picrate of (II), (6) molecular refraction (the observed molecular refraction, 47.75, agreed more closely with that calculated[3] for (IIa), 47.76, than with that for an N-alkene lactamide, 48.72), and (7) analogy with the work of Smith and Adkins,[4] who attempted to distil N-(1,1-dimethyl-3-hydroxybutyl)-acetamide at 130–140°, and obtained instead 2,4,4,6-tetramethyl-5,6-dihydro-1,3,4H-oxazine.

The two methyl groups on the carbon adjacent to the amide nitrogen promote the dehydration of (I) to (II), for N-(3-hydroxybutyl)-lactamide (which lacks these two methyl groups) was distilled in a tensimeter-still[5] without difficulty.

Experimental[6]

Materials.—The methyl lactate, a commercial material, was redistilled in vacuum. The 4-methyl-4-amino-2-pentanol was distilled in vacuum in an efficient still; b. p. 83° (22 mm.); $n^{20}D$ 1.4362; neut. equiv., 116.4 (calcd., 117.2).

4,4,6-Trimethyl-2-(1-hydroxyethyl)-5,6-dihydro-1,3,-4H-oxazine.—To 128 g. (1.1 moles) of the amine was added 104 g. (1.0 mole) of methyl lactate; after storage at room temperature for seven days, a sample of the mixture showed 97% reaction. Methanol and excess amine (and possibly water) were removed under vacuum (Vigreux column); the pressure was gradually lowered so that the temperature of the liquid did not exceed 130°. The remaining liquid was transferred to the tensimeter-still. It had a higher vapor pressure than expected; it distilled at 92° (14.5 mm.) to 97° (9.5 mm.) in 90% yield (computed as (II)). The temperature of the liquid did not exceed 130°. After redistillation twice in vacuum (Vigreux column), b. p. 97° (18.5 mm.), the following properties were determined: $n^{20}D$ 1.4481; d^{20}_4 0.9679; neut. equiv. (in ice-water), 171.6, 171.1 (basic). *Anal.* Calcd. for $C_9H_{17}O_2N$: C, 63.1; H, 10.0; N, 8.18; neut. equiv., 171.2; OH, 9.9. Found: C, 63.1; H, 10.2; N, 8.08; OH, 10.5.[7]

Base Picrate.—The picrate of (II) was formed in good yield by treatment with picric acid in benzene, and was recrystallized thrice from benzene, m. p. 147°. *Anal.* Calcd. for $C_{15}H_{20}O_9N_4$: C, 45.0; H, 5.04; N, 14.0. Found: C, 45.7; H, 5.18; N, 13.8. A picrate of 4-methyl-4-amino-2-pentanol was prepared, m. p. 146–147°; mixed m. p. with the oxazine picrate 120–125°.

Attempts to characterize (II) through the 3,5-dinitrobenzoate and the *p*-nitrobenzoate were unsuccessful; the former was a gummy mass and the latter an oil. Toward benzenesulfonyl chloride, (II) was unreactive.

Hydrolysis of (II) to (I).—To an 8.0-g. (0.047 mole) sample of (II) was added 0.85 g. (0.047 mole) of water. After ten days, the mixture solidified. It was recrystallized thrice from ether–ethanol, m. p. 93–95.5°; mixed m. p. with authentic (I) 93–93.5°. *Anal.* Calcd. for $C_9H_{19}O_3N$: N, 7.40. Found: N, 7.36.

N-(1,1-Dimethyl-3-hydroxybutyl)-lactamide (I).—The aminolysis reaction was repeated, using 1 mole each of ester and amine; after sixteen days, titration indicated 89% reaction. An aliquot was seeded with (I) and cooled; it became a semi-solid mass. This was filtered, and the solid was crystallized once from ether–ethanol yielding 12% of crude (I) (m. p. 88–90°). The crude (I) was recrystallized several times from ether–ethanol, m. p. 94–95.5°. *Anal.* Calcd. for $C_9H_{19}O_3N$: C, 57.1; H, 10.1; OH, 18.1. Found: C, 56.8; H, 10.0; N, 7.52; OH, 18.5.[7]

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(1) Contribution from one of the Laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(2) Ratchford, *Ind. Eng.Chem.*, in press.

(3) Using 4.10 for the atomic refraction of N in the group C—N=C of (IIa) (von Auwers, *Z. physik. Chem.*, **147**, 436 (1930)); 2.76 for N in the unsaturated lactamide (D'Alelio and Reid, This Journal, **59**, 109-111 (1937)), and the customary values for the other atoms (Gilman, "Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751).

(4) Smith and Adkins, This Journal, **60**, 407 (1938).

(5) Ratchford and Rehberg, *Anal. Chem.*, **21**, 1417 (1949).

(6) All melting points are uncorrected.

(7) Hydroxyl determination by the method of Ogg, Porter and Willits, *Ind. Eng. Chem., Anal. Ed.*, **17**, 394 (1945).